UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,443	10/14/2005	Xin Xie	514572000700	3904

25225 7590 10/17/2008

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
MUMMERT, STEPHANIE KANE	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
10/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,443	XIE ET AL.	
	Examiner	Art Unit	
	STEPHANIE K. MUMMERT	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13,18-29 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,18-29 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/12/08;5/15/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on June 3, 2008 is acknowledged and has been entered. Claims 1 and 32 have been amended. Claims 14-17, 30-31 and 35-36 have been canceled. Claims 1-13, 18-29 and 32-34 are pending.

Claims 1-13, 18-29 and 32-34 are discussed in this Office action.

All of the amendments and arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons discussed below. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

This action is made FINAL.

New Grounds of Rejection

Information Disclosure Statement

The information disclosure statements (IDS) submitted on May 15, 2008 and August 12, 2008 were filed in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 11-13, 18-25, 27-28 and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Dzieglewska (WO98/51693). Dzieglewska teaches a method of isolating nucleic acids from a sample of cells (Abstract).

With regard to claim 1, Dzieglewska teaches a process for amplifying a nucleic acid of a target cell or virus, which process comprises:

a) contacting a sample containing or suspected of containing a target cell or virus with a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity (p. 5-6, where target cells or viruses are contacted with a solid support which attaches to the solid support non-specifically, through hydrophobic or hydrophilic interactions, for instance; p. 10, lines 8-28, where magnetic particles are preferred);

b) allowing said target cell or virus, if present in said sample, to bind to said magnetic microbead to form a conjugate between said target cell or virus and said magnetic microbead (p. 10, lines 8-28, where the cell binds to the magnetic bead); and

c) separating said conjugate from other undesirable constituents via a magnetic force to isolate said target cell or virus from said sample (p. 10, lines 8-28, where the cells bind to the magnetic bead and they are separated away from the sample); and

d) applying said separated conjugate to a nucleic acid amplification system to amplify a

nucleic acid from said target cell or virus (p. 15, lines 16-20, where the separated conjugate is treated to release the nucleic acids and the nucleic acids are used in an amplification reaction) wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof (p. 5-6, where the target cells attach or bind to the particles in a variety of ways which are not mediated through a biomolecule or through specific interaction).

With regard to claim 2, Dzieglewska teaches an embodiment of claim 1, wherein the sample is a clinical sample (p. 4, lines 35-37, where the cells may be obtained from clinical, food or environmental samples).

With regard to claim 3, Dzieglewska teaches an embodiment of claim 1, wherein the sample is selected from the group consisting of serum, plasma, whole blood, sputum, cerebral spinal fluid, amniotic fluid, urine, gastrointestinal contents, hair, saliva, sweat, gum scrapings, marrow, tissue and cell culture (p. 5, where the sample may include a biological sample such as whole blood, plasma, feces).

With regard to claim 4, Dzieglewska teaches an embodiment of claim 1, wherein the target cell is selected from the group consisting of an animal cell, a plant cell, a fungus cell, a bacterium cell, a recombinant cell and a cultured cell (p. 5, where the target cell may include animal cells, plant cells, fungal cells).

With regard to claim 5, Dzieglewska teaches an embodiment of claim 1, wherein the target virus is an eucaryotic cell virus or a bacteriophage (p. 5, where the target cell can include a bacteriophage or other virus).

With regard to claim 6, Dzieglewska teaches an embodiment of claim 1, wherein the magnetic microbead comprises a magnetizable substance selected from the group consisting of a paramagnetic substance, a ferromagnetic substance and a ferrimagentic substance (p. 10, lines 29-36, where the magnetic microbeads comprise a paramagnetic substance).

With regard to claim 11, Dzieglewska teaches an embodiment of claim 1, wherein the magnetic microbead has a diameter ranging from about 5 to about 50,000 nanometers (p. 9, lines 26-33, where the bead has a diameter of 1-2 um).

With regard to claim 12-13, Dzieglewska teaches an embodiment of claim 1, wherein the magnetic microbead is untreated or modified with an organic molecule such as hydroxyl, carboxyl or epoxy (p. 10-11, where the bead can be modified with functional groups).

With regard to claim 18 and 33, Dzieglewska teaches an embodiment of claim 1 and 32, which further comprises washing the separated conjugate to remove the undesirable constituents before applying separated conjugate to a nucleic acid amplification system (p. 14, lines 31-35, where the conjugate is washed before further processing or analysis).

With regard to claim 19, Dzieglewska teaches an embodiment of claim 1, which is automated (p. 16, lines 12-14, where the method can be amenable to automation).

With regard to claim 20, Dzieglewska teaches an embodiment of claim 1, which is completed within a time ranging from about 0.5 minute to about 30 minutes (p. 16, lines 1-11, where it is noted that the method can be carried out in less than an hour or less than 45 minutes, which is about 30 minutes).

With regard to claim 21, Dzieglewska teaches an embodiment of claim 1, which is conducted in an eppendorf tube (p. 20, Example 1, where the method is conducted in a microfuge tube).

With regard to claim 22, Dzieglewska teaches an embodiment of claim 1, which is conducted in the absence of a precipitation or centrifugation procedure (p. 15, where the advantage of using beads allows for easy washing steps by agreggating the particles and where it is noted that the nucleic acid bound to the particles can be used without elution in amplification analysis).

With regard to claim 23, Dzieglewska teaches an embodiment of claim 1, which is conducted in the absence of a poisonous agent (Example 1, p. 20, where no poisonous agents are incorporated into the method).

With regard to claim 24, Dzieglewska teaches an embodiment of claim l, which is conducted at an ambient temperature ranging from about 0°C to about 35°C without temperature control (p. 20, Example 1, where the method is carried out primarily at room temperature, or ambient temperature).

With regard to claim 25, Dzieglewska teaches an embodiment of claim 1, wherein the sample volume ranges from about 5 ul to about 50 ul (p. 20, Example 1, where a variety of volumes are used in the practice of the method, including 20 ul and 50 ul volumes).

With regard to claim 27, Dzieglewska teaches an embodiment of claim 1, wherein the target cell is an epithelia cast-off cell or a bacteria cell isolated from saliva, urine and tissue culture (p. 5, where the target cell can comprise a bacteria or eukaryotic cell and can be obtained from biological samples including urine).

With regard to claim 28, Dzieglewska teaches an embodiment of claim 1, wherein the nucleic acid amplification system is selected from the group consisting of polymerase chain reaction (PCR), ligase chain reaction (LCR), nucleic acid sequence-based amplification (NASBA), strand displacement amplification (SDA) and transcription-medicated amplification (TMA) (p. 15, lines 16-20, where the separated conjugate is treated to release the nucleic acids and the nucleic acids are used in an amplification reaction, including PCR).

With regard to claim 32, Dzieglewska teaches a process for amplifying a nucleic acid of a target cell or virus, which process comprises:

a) contacting a sample containing or suspected of containing a target cell or virus with a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity (p. 5-6, where target cells or viruses are contacted with a solid support which attaches to the solid support non-specifically, through hydrophobic or hydrophilic interactions, for instance; p. 10, lines 8-28, where magnetic particles are preferred);

b) allowing said target cell or virus, if present in said sample, to bind to said magnetic microbead to form a conjugate between said target cell or virus and said magnetic microbead (p. 10, lines 8-28, where the cell binds to the magnetic bead); and

c) separating said conjugate from other undesirable constituents via a magnetic force to isolate said target cell or virus from said sample (p. 10, lines 8-28, where the cells bind to the magnetic bead and they are separated away from the sample);

d) releasing a nucleic acid from said cell-microbead or virus-microbead conjugate to form a nucleic acid-microbead conjugate (p. 15, lines 16-20, where the separated conjugate is treated to release the nucleic acids and the nucleic acids); and

g-)e) applying said nucleic acid-microbead conjugate to a nucleic acid amplification system to amplify said nucleic acid from said target cell or virus (p. 15, lines 16-20, where the separated conjugate is treated to release the nucleic acids and the nucleic acids are used in an amplification reaction);

wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof (p. 5-6, where the target cells attach or bind to the particles in a variety of ways which are not mediated through a biomolecule or through specific interaction).

With regard to claim 34, Dzieglewska teaches an embodiment of claim 32, which further comprises separating nucleic acid-microbead conjugate from other undesirable constituents via a magnetic force before applying the nucleic acid-microbead conjugate to a nucleic acid amplification system (p. 15, lines 16-20, where the separated conjugate is treated to release the nucleic acids and the nucleic acids are used in an amplification reaction).

Claim Rejections - 35 USC § 103

Claims 7-10 are rejected under 35 U.S.C. 103(a) as being obvious over Dzieglewska (WO98/51693) as applied to claims 1-6, 11-13, 18-25, 27-28 and 33-34 and further in view of Ughelstad et al. (WO83/03920; November 1983). Dzieglewska teaches a method of isolating nucleic acids from a sample of cells (Abstract).

Regarding magnetic beads, Dzieglewska teaches that the beads can comprise Dynabeads, but does not teach details about their composition. Ughelstad teaches the details of the process of forming magnetic particles (Abstract).

With regard to claim 7, Ughelstad teaches an embodiment of claim 6, wherein the magnetizable substance comprises a metal composition (p. 8-9, where the particles comprise metal iron oxide).

With regard to claim 8, Ughelstad teaches an embodiment of claim 7, wherein the metal composition is a transition metal composition or an alloy thereof (p. 8-9, where the particles comprise metal iron oxide).

With regard to claim 9, Ughelstad teaches an embodiment of claim 8, wherein the transition metal is selected from the group consisting of iron, nickel, copper, cobalt, manganese, tantalum, zirconium and cobalt- tantalum-zirconium (CoTaZr) alloy (p. 8-9, where the particles comprise metal iron oxide).

With regard to claim 10, Ughelstad teaches an embodiment of claim 7, wherein the metal composition is Fe304 (p. 9, where the metal comprises Fe3O4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the specific teachings of Ughelstad to the particles of Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. As taught by Dzieglewska, "especially preferred are superparamagnetic particles, for example those described by Sintef in EP-A-106873" (the WO83/03920 replaced the prior document). However, the sole disclosure of Dzieglewska does not anticipate the beads as claimed because the detailed description is provided elsewhere. Regarding these preferred particles, "magnetic polymer

particles are spherical and have a uniform concentration of magnetic material. They may be used for medical, diagnostic, or other purposes" (Abstract). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the specific teachings of Ughelstad to the particles of Dzieglewska to arrive at the claimed invention with a reasonable expectation for success.

Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dzieglewska (WO98/51693) as applied to claims 1-6, 11-13, 18-25, 27-28 and 33-34 above and further in view of Inuma et al. (Int. J. Cancer, 2000, vol. 89, p. 337-344). Dzieglewska teaches a method of isolating nucleic acids from a sample of cells (Abstract).

Dzieglewska teaches all of the limitations of claims 1-6, 11-13, 18-25, 27-28 and 33-34 as recited in the 102 rejection stated above. While Dzieglewska teaches that cells can be isolated from blood, regarding claim 26, Dzieglewska does not teach that the cells comprise leukocytes. Inuma teaches that leukocytes can be specifically targeted by magnetic beads comprising antibodies (p. 337, col. 2).

With regard to claim 26, Inuma teaches an embodiment of claim 1, wherein the target cell is a leukocyte isolated from whole blood, marrow or lympha (p. 337, col. 2, where 'anti-CD45 Mab-conjugated microbeads... bind to a common antiden of leukocytes').

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have analyzed the target cells of Inuma using the method of separation taught by Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. As taught by Inuma, "prepared cells were resuspended in 80 µl of BSA-PBS mixed

with 20 μl of CD45 microbeads for 15 min at 4°C and passed down the MACS column" (p. 338, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have analyzed the target cells of Inuma using the method of separation taught by Olsvik to arrive at the claimed invention with a reasonable expectation for success.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dzieglewska (WO98/51693) as applied to claims 1-6, 11-13, 18-25, 27-28 and 33-34 above, and further in view of Lopez-Sabater et al. (Letters in Applied Microbiology, 1997, vol. 24, p. 101-104).

Dzieglewska teaches all of the limitations of claims 1-6, 11-13, 18-25, 27-28 and 33-34 as recited in the 102 rejection stated above. However, Dzieglewska does not teach removing cells suspected of containing a virus before contacting the sample with microbeads. Lopez-Sabater teaches a method for the magnetic immunoseparation for detection of viral sequences by PCR (Abstract).

With regard to claim 29, Lopez-Sabater teaches an embodiment of claim 1, which further comprises removing cells from a sample containing or suspected of containing a target virus or bacteriophage before contacting the sample with a magnetic microbead (p. 102, col. 1, 'recovery' heading, where the oyster cells were diced and homogenized, therefore the cells were removed before contacting with a magnetic microbead).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the technique of homogenization of a sample suspected of containing a virus as taught by Lopez-Sabater to the method of isolation and analysis taught by Dzieglewska to arrive at the claimed invention with a reasonable expectation for success. As

taught by Lopez-Sabater, "samples (20g) of shucked American oyster… were inoculated with levels of HAV ranging from 10 to 10^3 pfu" and "after 1 hour at room temperature, artificially contaminated oysters were diced with sterile scissors" and subsequently homogenized (p. 102, col. 1). Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to have applied the technique of homogenization of a sample suspected of containing a virus as taught by Lopez-Sabater to the method of isolation and analysis taught by Dzieglewska to arrive at the claimed invention with a reasonable expectation for success.

Response to Arguments

Applicant's arguments with respect to claims 1-13, 18-29, 32-34 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Hardingham et al. (Cancer Research, 1993, vol. 53, p. 3455-3458) teaches a general method for immunobead isolation of circulating tumor cells followed by PCR (Abstract).

No claims are allowed. All claims stand rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEPHANIE K. MUMMERT whose telephone number is (571)272-8503. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephanie K. Mummert/
Patent Examiner, Art Unit 1637

/GARY BENZION/
Supervisory Patent Examiner, Art Unit 1637